Method for producing imidazolium salts

The invention relates to a process for preparing imidazolium salts by reacting bisimines or corresponding heterocycles with a combination of an alkylating agent and a metal salt as a promoter of the reaction. This process allows the preparation of a multitude of imidazolium salts under mild reaction conditions and in good yields. This synthetic process makes it possible to prepare new types of imidazolium salts of the general formulae II, IV and XI (especially chiral enantiomerically pure and highly substituted imidazolium salts), and also already known imidazolium salts of the general formula VI with an improved yield. The imidazolium salts may be converted by deprotonation to N-heterocyclic carbenes and transition metal complexes thereof. These complexes have a high thermal and chemical stability, and very good homogeneous catalyst properties for various reactions.

The use of N-heterocyclic carbenes of the imidazole type as ligands in homogeneous transition metal catalysis has become a significant field of research. Particularly processes for C-C-, C-O- and C-N-bond formation and applications in olefin metathesis have gained great significance. These include in particular successful applications in Heck, Suzuki, Sonogashira, Kumada and Stille cross-couplings, aryl aminations, α-arylations of amides, hydrosilylations, hydrogenations, 1,4-additions, hydroformylations, cyclopropanations of olefins, arylations and alkenylations of aldehydes, reductions of haloarenes, free-radical atom transfer polymerizations, olefin metathesis, ethylene/carbon monoxide copolymerizations, C-H activations and telomerizations of 1,3-dienes with alcohols. For example, DE 4447067 A1 describes cobalt and rhodium complexes having heterocyclic mono- or dicarbene ligands as catalysts for

the industrially important hydroformylation. Industrial interest is also attracted by free-radical atom transfer polymerization, for which an iron(II)-carbene complex exhibits the currently highest polymerization rates observed in solvents with simultaneously low polydispersity. Additionally of particular significance are the numerous applications of ruthenium complexes of N-heterocyclic carbenes in olefin metathesis, which has clearly shown the advantages of N-heterocyclic carbene ligands over phosphane ligands, for example in DE 1981527.5.

The total sales of enantiomerically pure pharmaceuticals grew for the first time in the year 2000 to above 100 billion dollars, so that there is a great demand for enantiomerically pure substances. Transition metal complexes of chiral, enantiomerically pure N-heterocyclic carbenes are promising catalysts in asymmetric catalysis. (Comprehensive Asymmetric Catalysis; Eds.: E.N. Jacobsen, A. Pfaltz, H. Yamamoto; Springer: Berlin, 1999.) The first very successful applications of such chiral complexes in the hydrogenation of trisubstituted alkenes and in olefin metathesis confirm this potential. At the present time, there exist only relatively few chiral imidazolium salts. (See, for example, C. Bolm, M. Kesselgruber, G. Raabe, Organometallics (2002) 21, 707; J.J. Van Veldhuizen, S.B. Garber, J.S. Kingsbury, A.H. Hoveyda, J. Am. Chem. Soc. (2002) 124, 4954; T.J. Seiders, D.W. Ward, R.H. Grubbs, Org. Lett. (2001) 3, 3225; M.T.Powell, D.-R. Hou, M.C. Perry, X. Cui, K. Burgess, J. Am. Chem. Soc. (2001) 123, 8878; S. Lee, J.F. Hartwig, J. Org. Chem. (2001) 66, 3402; D.S. Clyne, J. Jin, E. Genest, J.C. Gallucci, T.V. RajanBabu, Org. Lett. (2000) 2, 1125.) The synthesis of novel, chiral imidazolium salts, especially imidazolium salts having a stereocenter directly adjacent, and the use of their transition metal complexes in asymmetric catalysis is

therefore of great significance.

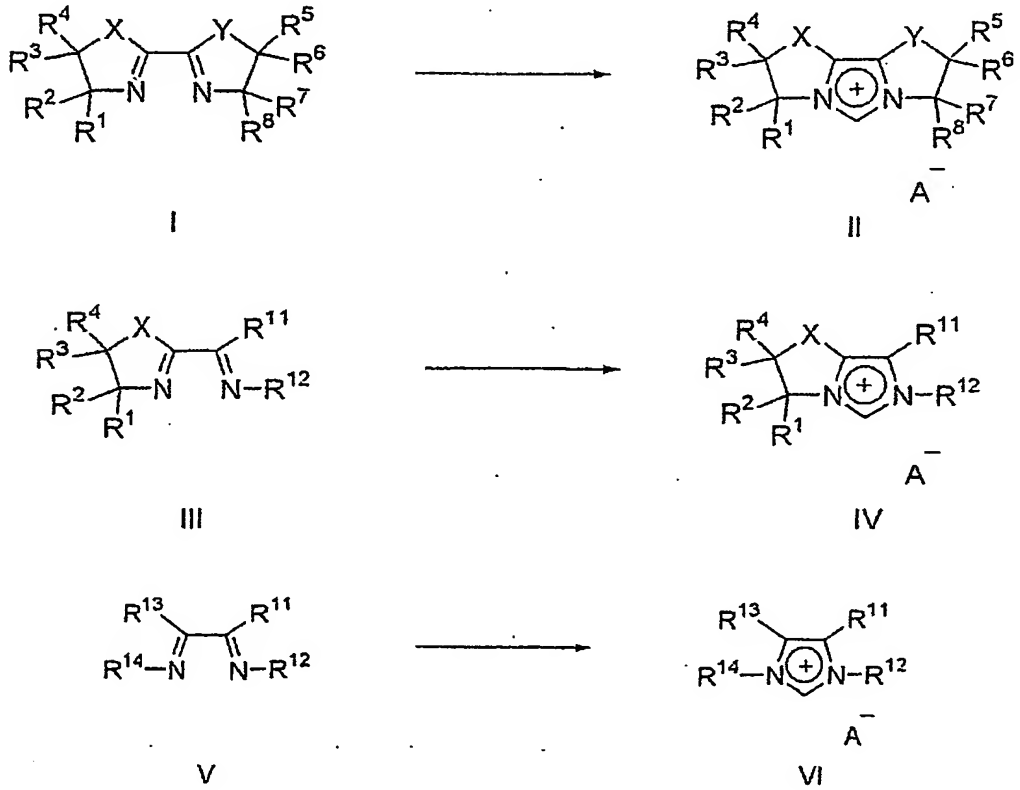
The deprotonation of imidazolium salts for the preparation of the corresponding N-heterocyclic carbenes and their transition metal complexes has found wide use as a method of choice. Generally usable synthetic methods for imidazolium salts are therefore of great interest. There already exist numerous synthetic methods for imidazolium salts. (Review: W.A. Herrmann, Angew. Chem. (2002) 114, 1342.) Starting from glyoxal, primary amines and formaldehyde, imidazolium salts can be formed under acidic reaction conditions (US Patent No. 5182405). Isolated bisimines obtained from glyoxal may likewise be reacted with acid and formaldehyde or with chloromethyl ethyl ether to give imidazolium salts (US Patent No. 5077414). Unsymmetric 1,3-disubstituted imidazolium salts may be obtained by alkylating monosubstituted imidazoles. The monosubstituted imidazoles required for this purpose may be obtained in analogy to the abovementioned synthesis from glyoxal, formaldehyde and a mixture of a primary amine with ammonium chloride. Saturated imidazolium salts may be obtained from substituted 1,2-bisamines by reaction with formaldehyde or trialkyl orthoformate.

Owing to their reaction conditions (usually in acidic medium, in the presence of nucleophiles and at relatively high temperature), the field of application of these synthetic methods is limited. The versatility of the substance classes suitable as a starting material is therefore restricted, so that numerous substitution patterns cannot be obtained with the known methods. In particular, it has hitherto not been possible to prepare many chiral imidazolium salts and imidazolium salts having acid-sensitive substituents. Among other compounds, the literature does not describe any examples of imidazolium salts of the general formulae II and IV. Furthermore, the above-described synthetic processes

afford frequently only moderate yields after frequently long reaction times.

It has been found that, surprisingly, using a combination of alkylating agent and a metal salt as a promoter of the reaction, it is possible for the first time to prepare under mild conditions the imidazolium salts of the general formulae II, IV and XI shown below, and to prepare the imidazolium salts of the general formula VI in improved yield.

The invention provides a process for preparing imidazolium salts of the general formulae II, IV and VI, comprising the reaction of the corresponding substrates I, III and V,



where

R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, R^{12}, R^{13} and R^{14} are the

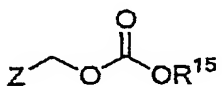
same or different and are saturated or unsaturated, straight-chain, branched or cyclic, unsubstituted or substituted C_{1-10}-alkyl, C_{2-5}-alkenyl, C_{2-5}-alkynyl, C_{7-19}-aralkyl or C_{6-14}-aryl substituents, or R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, R^{12} and R^{13} may also be hydrogen or, together, form fused, substituted or unsubstituted substituents having 3-7 carbon atoms, R^{11} and R^{13} may also be $-OR^{16}$, $-SR^{17}$ or $-NR^{18}R^{19}$, in which R^{16}, R^{17}, R^{18} and R^{19} may each be as defined for the R^1 to R^8 and R^{11} to R^{14} substituents, and R^{16}, R^{17}, R^{18}, R^{19} and one of the R^1, R^2, R^7, R^8, R^{12} and R^{14} substituents may also be a linker L to a further imidazolium salt of the formula II, IV or VI,

X is O, S, an NR^9 or $CR^{9a}R^{9b}$ group in which R^9, R^{9a} and R^{9b} are each hydrogen, saturated or unsaturated, straight-chain, branched or cyclic, unsubstituted or substituted C_{1-10}-alkyl, C_{2-5}-alkenyl, C_{2-5}-alkynyl, C_{7-19}-aralkyl or C_{6-14}-aryl substituents,

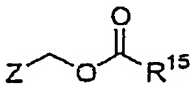
Y is O, S, an NR^{10} or $NR^{10a}R^{10b}$ group in which R^{10}, R^{10a}, R^{10b} are hydrogen, saturated or unsaturated, straight-chain, branched or cyclic, unsubstituted or substituted C_{1-10}-alkyl, C_{2-5}-alkenyl, C_{2-5}-alkynyl, C_{7-19}-aralkyl or C_{6-14}-aryl substituents, and

A^- is a mono- or polyvalent, organic or inorganic anion or a metal complex ion

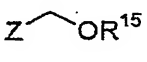
with a combination of an alkylating agent of the general formula VII, VIII or IX



VII



VIII



IX

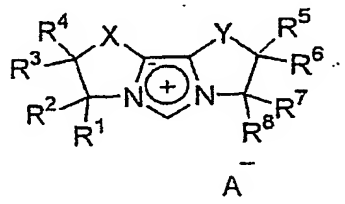
where Z is a leaving group and R^{15} is as defined for R^3, and a metal salt of the general formula

MA

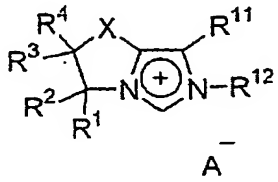
where M is a mono- or polyvalent metal cation, a tetraorganoammonium compound or a triorganosilyl group,

and A is as defined above for A^- as a promoter of the reaction.

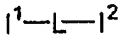
The present invention further provides compounds of the general formulae II, IV and XI



II



IV



XI

where

I^1 and I^2 are identical or different imidazolium salts of the formulae II, IV and VI which are joined to L at the position of the R^1, R^2, R^7, R^8, R^{12} or R^{14} substituents, with the proviso that I^1 and I^2 are not both an imidazolium salt of the formulae VI,

the imidazolium salt of the formula VI, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, R^{12}, R^{13}, R^{14}, X, Y, L and A^- are each as defined above.

In one possible embodiment, R^{11} and R^{12} are joined together to form a substituted or unsubstituted cycle, preferably to form a pyridyl ring. Preferred substituents are C_{1-6}-alkyl and C_{6-14}-aryl. The substituents are preferably bonded to the carbon adjacent to the ring nitrogen.

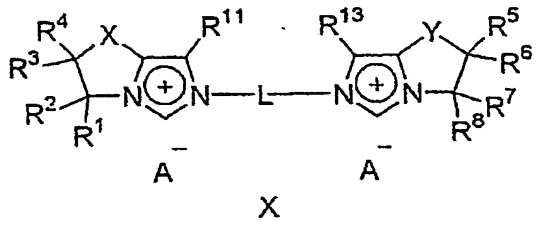
In the above-defined compounds, it is preferred that R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{9a}, R^{9b}, R^{10a}, R^{10b}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, are the same or different and are each saturated or unsaturated, straight-chain, branched or cyclic, unsubstituted or substituted C_{1-6}-alkyl, C_{2-4}-alkenyl, C_{2-4}-alkynyl, C_{7-10}-aralkyl or phenyl groups.

The C_{1-6}-alkyl substituents may be selected from methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, n-pentyl, i-pentyl, t-pentyl, n-hexyl, i-hexyl, t-hexyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl. The C_{2-4}-alkenyl substituents may be selected from ethenyl, propenyl or butenyl, the C_{2-4}-alkynyl substituents from ethynyl, propynyl or butynyl. The C_{7-10}-aralkyl substituents may be selected from benzyl, phenylethyl, phenylpropyl and phenylbutyl.

The R^1 to R^{19} substituents may be substituted by one or more, identical or different amine, nitro, nitrile, isonitrile, ether, alcohol, aldehyde or ketone groups, carboxylic acid derivatives, in particular esters or amides, halogenated, in particular fluorinated or perfluorinated, hydrocarbon substituents, carbohydrate, phosphane, phosphane oxide, phosphane sulfide, phosphole groups, phosphite derivatives, aliphatic or aromatic sulfonic acid derivatives, the salts, esters or amides thereof, silyl functions, boryl groups or heterocyclic substituents. Further suitable substituents, especially when they are aromatic systems, are C_1-C_6-alkyl, C_2-C_4-alkenyl or C_2-C_4-alkynyl groups. In a particularly preferred embodiment, one of the R^1, R^2, R^7, R^8, R^{12} and R^{14} groups is substituted by an azolium salt or a pyridine ring.

In a further embodiment, one of the R^1, R^2, R^7, R^8, R^{12} and R^{14} substituents is a linker L to a further imidazolium salt of the formula II, IV or VI. L may in particular be a C_{1-4}-alkylene group, (e.g. a methylene, ethylene, propylene or butylene group), a C_{5-12}-cycloalkylene group (e.g. a 1,2- or 1,4-cyclohexylene group), a C_{6-12}-arylene group (e.g. a 1,2-, 1,3- or 1,4-phenylene group) or a C_{6-12}-heteroarylene group (e.g. a 2,3-, 2,4- or 2,6-pyridinylene group). The

aforementioned groups may optionally be substituted (for example by C_{1-4}-alkyl groups, C_{1-4}-alkoxy groups, halogen atoms, hydroxyl groups, etc.) or be interrupted by a heteroatom (e.g. O or NH) or a cyclic groups (e.g. a phenyl or cyclohexyl groups). Particular preference is given to an imidazolium salt which has the general formula X



X

where the variables are each as defined above.

It is also preferred that the mono- or polyvalent organic anion A^- in the general formulae II, IV, VI and XI is a sulfate, halide, pseudohalide, borate, phosphate or metal complex ion or an optionally halogenated sulfonate, carboxylate or acetylacetonate ion, and A^- is in particular a triflate, mesylate, tosylate, nonaflate, tresylate, benzenesulfonate, brosylate, nosylate, fluorosulfonate, tetraphenylborate, tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BARF), tetrafluoroborate, hexafluorophosphate, hexafluoroantimonate, acetate, trifluoroacetate, perchlorate, tetracarbonylcobaltate or hexafluoroferrate(III) ion. The particularly preferred anion among the anions A^- mentioned is the triflate ion.

The process (1) includes the use of an alkylating agent of the above-defined general formula VII, VIII or IX. The leaving group Z in this alkylating agent is preferably a halide, pseudohalide or (optionally halogenated) carboxylate, more preferably a halide, more preferably a chloride. Preferred alkylating agents are

those in which R^{15} is an unsubstituted or substituted phenyl, benzyl or C_{1-4}-alkyl substituents which may in each case contain one or more substituents, in particular ether, ester or silyl substituents. Particular preference is given to chloromethyl pivalate, chloromethyl butyrate, chloromethyl ethyl ether, (2-methoxyethoxy)methyl chloride and (2-chloromethoxyethyl)trimethylsilane.

Preferred metal salts of the general formula MA which can be used in the process (1) are those in which the mono- or polyvalent metal cation M is a silver(I), alkali metal and alkaline earth metal, lanthanide, lead(II), mercury(II), cadmium(II), thallium(I), copper(II), zinc(II) or aluminum(III) ion, and those in which the tetraorganoammonium compound is a tetraalkylammonium compound and finally those in which the triorganosilyl group is a trialkylsilyl group. Particularly preferred metal salts are those in which M is silver(I) and A is a sulfonate, sulfate, halide, pseudohalide, oxide, borate, phosphate, carboxylate, acetylacetonate or metal complex ion, preferably a trifluoromethanesulfonate (triflate), methanesulfonate (mesylate), p-toluenesulfonate (tosylate), nonafluorobutanesulfonate (nonaflate), 2,2,2-trifluoroethanesulfonate (tresylate), benzenesulfonate, p-bromobenzenesulfonate (brosylate), p-nitrobenzenesulfonate (nosylate), fluorosulfonate, tetraphenylborate, tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BARF), tetrafluoroborate, hexafluorophosphate, hexafluoroantimonate, acetate, trifluoroacetate, perchlorate, tetracarbonylcobaltate or hexafluoroferrate(III) ion, and is more preferably a triflate ion.

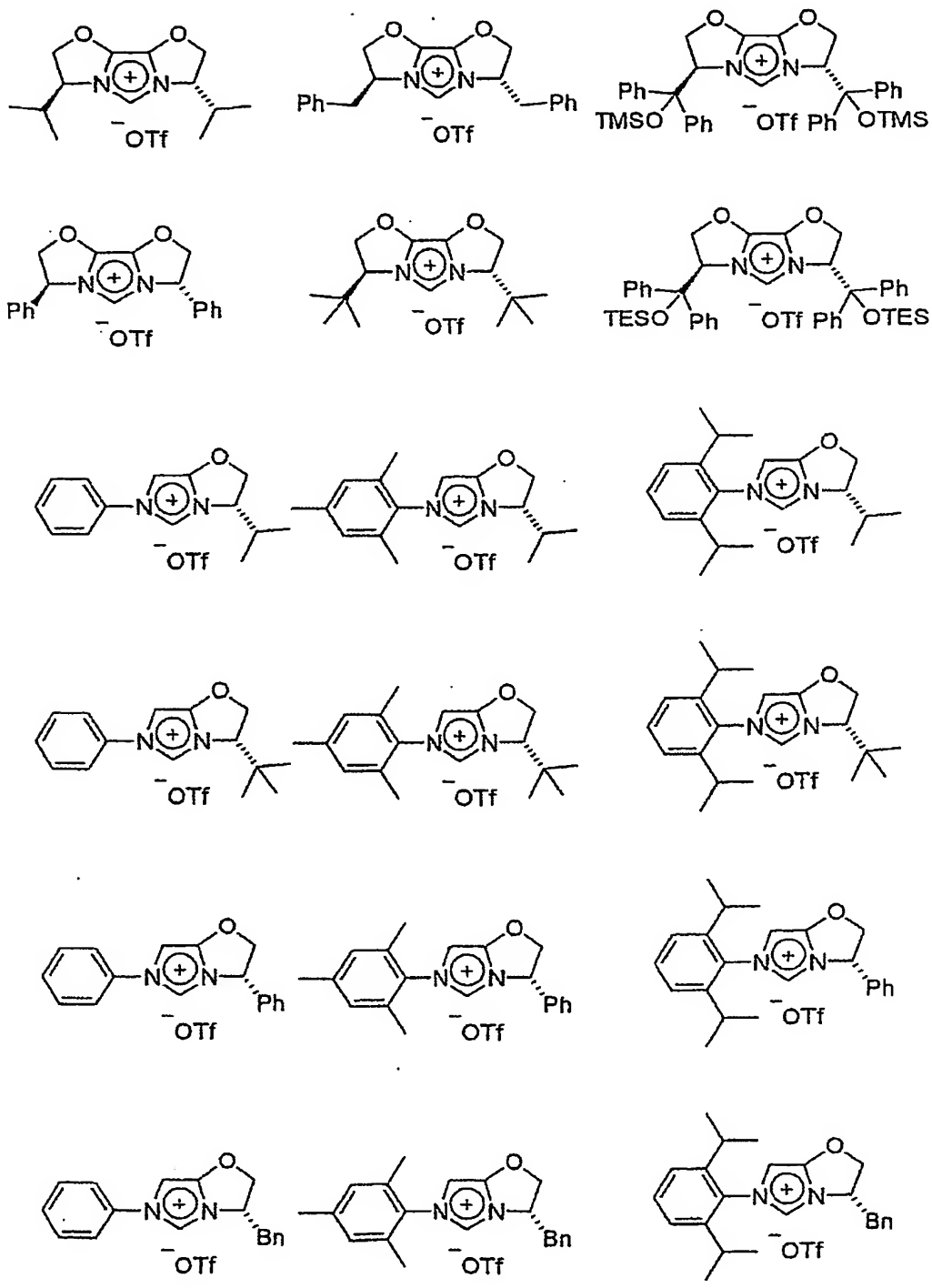
Typically, alkylating agent and metal salt are used in at least stoichiometric amount, preferably in a from 5 to 100% excess in relation to the substrate. The ratio

of alkylating agent to metal salt may be varied within a wide range and is preferably from 2:1 to 1:2, more preferably from 1.2:1 to 1:1.2.

The imidazolium salts of the general formulae II, IV and VI are synthesized preferably with the exclusion of air and moisture. It has been found to be particularly advantageous to add the alkylating agent to a solution of the appropriate starting material of the general formula I, III or V and the metal salt in an organic solvent. Suitable solvents may be acetone, tetrahydrofuran, diethyl ether, methyl *tert*-butyl ether, 1,2-dimethoxyethane, 1,4-dioxane, petroleum ether, dimethyl sulfoxide, *N*,*N*-dimethylformamide, 1-methyl-2-pyrrolidone, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidone, acetonitrile, propionitrile, ethyl acetate, benzene, toluene, xylene, benzine, chloroform, 1,2-dichloroethane and methylene chloride, preferably methylene chloride. After stirring at from -78 to 120°C, preferably at from 0 to 70°C, in particular at from 20 to 50°C, for a few hours, the reaction solution is purified in a conventional manner depending on the physical properties of the products, for example by column chromatography or crystallization.

The inventive imidazolium salts of the present invention are in particular those compounds in which R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, X, Y, L and A^- each have the preferred definition specified above.

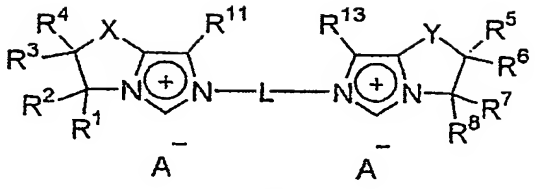
Particular preference is given to compounds having the following structural formulae:



where OTf is trifluoromethanesulfonate (triflate), Ph is phenyl, TMS is trimethylsilyl, TES is triethylsilyl and Bn is benzyl.

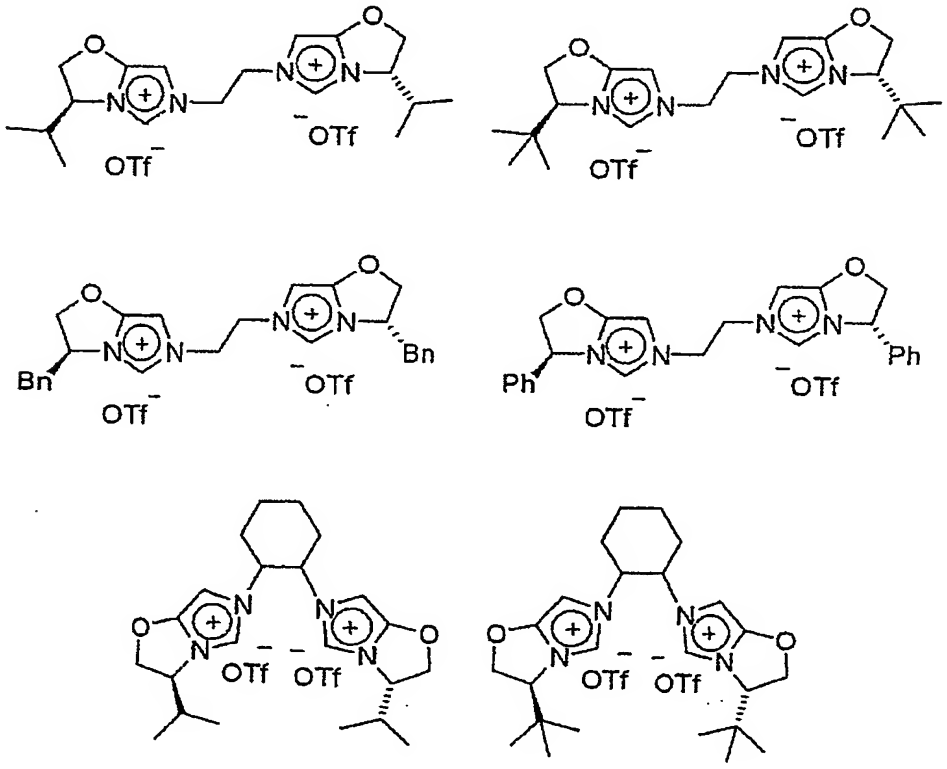
Preference is further given to the following compounds

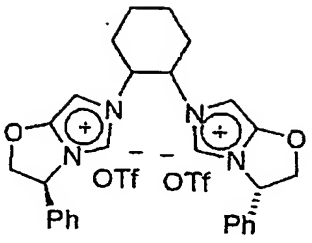
of the formula X

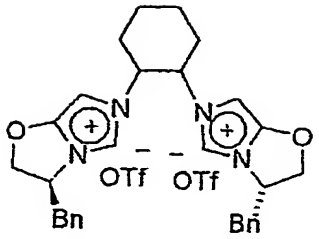


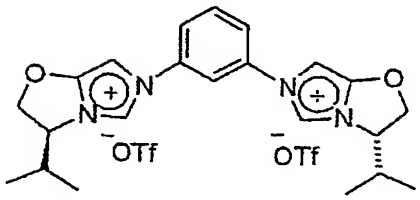
X

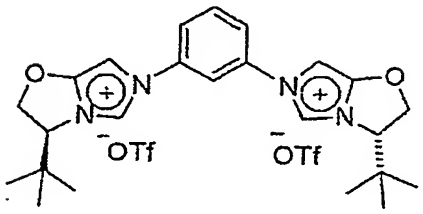
where each variable is as defined above. Among these, preference is given particularly to compounds having the following structural formulae:




OTf
OTf
Ph
Ph


OTf
OTf
Bn
Bn


OTf
OTf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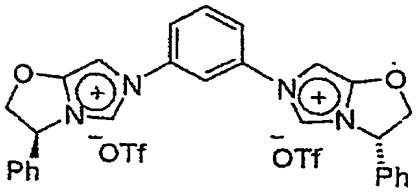
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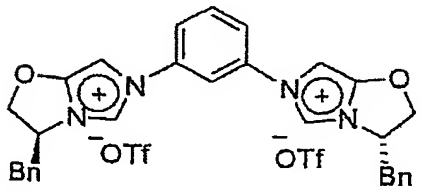
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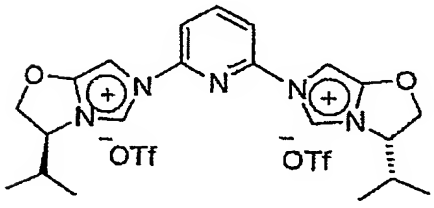
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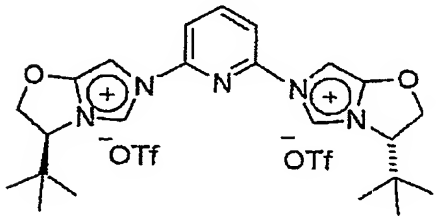
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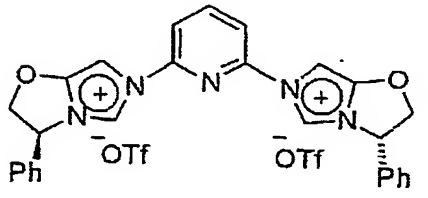
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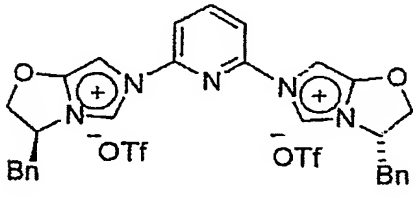
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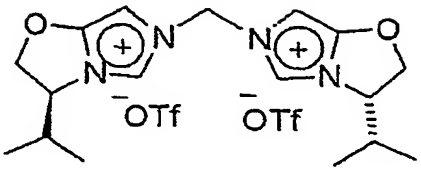
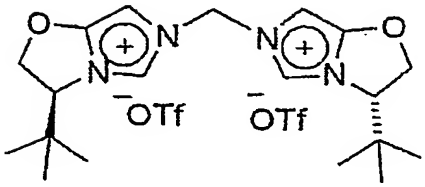
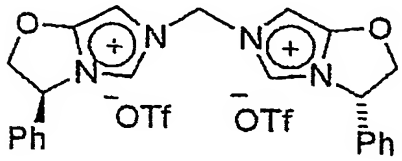
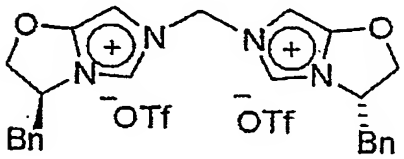








where OTf is trifluoromethanesulfonate (triflate), Ph is phenyl and Bn is benzyl.

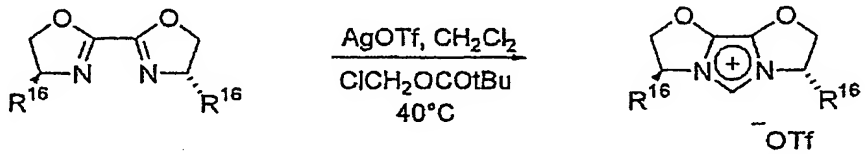
The compounds mentioned specifically above may likewise have tetrafluoroborate, mesylate, tosylate, nonaflate or hexafluoroantimonate instead of triflate as the counteranion.

The process according to the invention enables the preparation of a multitude of hitherto unknown, achiral and chiral imidazolium salts in surprisingly good yield, high purity and, if appropriate, high optical purity. This can be attributed firstly to the wide structural variety of the starting materials of the general formulae I, III and V and secondly to the mild alkylation conditions which surprisingly become possible as a result of the combined use of an alkylating agent and a metal salt as a promoter. The process according to the invention has therefore been found to be particularly useful for preparing imidazolium salts from acid-sensitive substrates and for the preparation of chiral imidazolium salts. In addition, the process can be used to synthesize both milligram and multigram amounts of imidazolium salts. Owing to the simple reaction, the process is also suitable for industrial application.

The imidazolium salts, preparable by this process, of the general formulae II, IV and VI can be deprotonated in accordance with the literature and thus converted to N-heterocyclic carbenes or transition metal complexes thereof. (Review: W.A. Herrmann, Angew. Chem. (2002) 114, 1342; A.J. Arduengo, III, Acc. Chem. Res. (1999) 32, 913.) These transition metal-carbene complexes may be used as catalysts in homogeneous catalysis, and chiral, enantiomerically pure imidazolium salts of the general formulae II, IV and VI lead to chiral transition metal complexes which can be used in particular in asymmetric catalysis. Especially the novel imidazolium salts of the general formulae II and IV in which the imidazolium ring is bridged by one ring (IV) or two rings (II) are promising in this context. Suitable substitution of these bridges with the R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 substituents allows chiral, enantiomerically pure imidazolium salts with rigid geometry to be obtained, whose transition metal-carbene complexes may find use in asymmetric catalysis.

Working examples

Conversion of bioxazolines **1** to the corresponding imidazolium triflates **2** according to the following equation.



1a: R^{16} = iPr
1b: R^{16} = tBu
1c: R^{16} = Ph

2a: R^{16} = iPr
2b: R^{16} = tBu
2c: R^{16} = Ph

Example 1

Preparation of imidazolium triflate **2a**

In a flame dried and argonized Schlenk vessel, with

exclusion of light, air and moisture, chloromethyl pivalate (4.6 ml, 31.2 mmol) was added to a solution of bioxazoline **1a** (5.0 g, 22.2 mmol) and silver triflate (6.8 g, 26.6 mmol) in methylene chloride (75 ml) and the reaction vessel was sealed. After stirring with exclusion of light at 40°C for 24 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, and the filter residue was washed with methylene chloride (25 ml) and the filtrate concentrated. Purification of the residue by column chromatography (4 × 10 cm, 20:1 CH_2Cl_2/MeOH) and subsequent recrystallization from THF (30 ml), toluene (150 ml) and pentane (50 ml) gave the imidazolium triflate **2a** (6.85 g, 80%).

$[a]^{20}_D$ = +55.0 (c 1.0, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H, NCHN), 5.07 (dd, *J* = 7.9, 9.0 Hz, 2H, CH_2), 4.98-4.93 (m, 2H, C*H*CH_2), 4.83 (dd, *J* = 4.1, 9.0 Hz, 2H, CH_2), 2.33 (m, 2H, C*H*CH_3), 1.03 (d, *J* = 6.9 Hz, 6H, CH_3), 0.99 (d, *J* = 6.9 Hz, 6H, CH_3), ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.6 (NCO), 120.6 (q, *J* = 320 Hz, CF_3), 116.3 (NCHN), 79.1 (CH_2), 63.9 (*C*HCH_2), 31.1 ($CHCH_3$), 17.6 (CH_3), 16.7 (CH_3), ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.7 (CF_3).

Example 2

Preparation of imidazolium triflate **2b**

In a flame dried and argonized Schlenk vessel, with exclusion of light, air and moisture, chloromethyl pivalate (0.35 ml, 2.4 mmol) was added to a solution of bioxazoline **1b** (425 mg, 1.7 mmol) and silver triflate (518 mg, 2.0 mmol) in methylene chloride (15 ml) and the reaction vessel was sealed. After stirring with exclusion of light at 40°C for 8 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, and the filter residue was washed with methylene chloride (10 ml) and the filtrate concentrated. Purification of the residue by column chromatography (2.5 × 10 cm, 20:1 CH_2Cl_2/MeOH) and subsequent recrystallization from THF (5 ml), toluene

(20 ml) and pentane (5 ml) gave the imidazolium triflate **2b** (521 mg, 75%).

$[a]^{20}_D$ = +69.5 (c 1.0, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H, NCHN), 5.07 (dd, J = 7.9, 9.3 Hz, 2H, CH_2), 4.92 (dd, *J* = 3.3, 9.4 Hz, 2H, CH_2), 4.83 (dd, *J* = 3.2, 7.8 Hz, 2H, CH), 1.08 (s, 18H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.9 (NCO), 120.6 (q, *J* = 320 Hz, CF_3), 117.0 (NCH), 78.8 (CH_2), 68.2 (CH), 34.1 (CCH_3), 25.3 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.6 (CF_3).

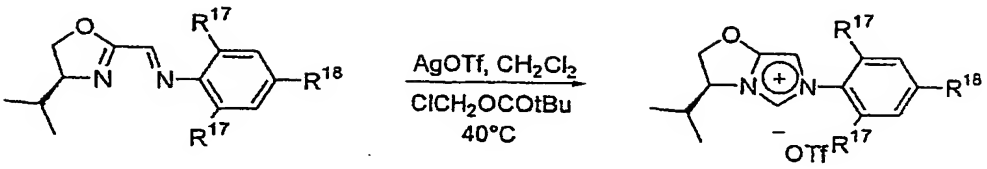
Example 3

Preparation of imidazolium triflate **2c**

In a flame dried and argonized Schlenk vessel, with exclusion of light, air and moisture, chloromethyl pivalate (0.85 ml, 5.8 mmol) was added to a solution of bioxazoline **1c** (1.2 g, 4.1 mmol) and silver triflate (2.6 g, 10.3 mmol) in methylene chloride (20 ml) and the reaction vessel was sealed. After stirring with exclusion of light at 40°C for 15 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, and the filter residue was washed with methylene chloride (10 ml) and the filtrate concentrated. Purification of the residue by double column chromatography (3 × 10 cm, 20:1 CH_2Cl_2/MeOH) gave the imidazolium triflate **2c** (430 mg, 23%).

$[a]^{20}_D$ = +226.3 (c 0.8, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H, NCHN), 7.42-7.31 (m, 10H, CH_{ar}), 6.05 (t, J = 7.2 Hz, 2H, CHPh), 5.41 (dd, *J* = 7.9, 8.9 Hz, 2H, CH_2), 4.90 (dd, *J* = 6.6, 9.0 Hz, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.4(C), 130.3 (CH) 129.8 (CH), 127.1 (CH), 126.6 (NCO), 120.6 (q, *J* = 320 Hz, CF_3), 114.9 (NCHN), 84.1 (CH_2), 62.2 (CHPh); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.6 (CF_3).

Conversion of imine oxazolines **3** to the corresponding imidazolium triflates **4** according to the following equation



3a: R^{17} = Me, R^{18} = Me
3b: R^{17} = iPr, R^{18} = H

4a: R^{17} = Me, R^{18} = Me
4b: R^{17} = iPr, R^{18} = H

Example 4

Preparation of imidazolium triflate **4a**

In a flame dried and argonized Schlenk vessel, with exclusion of light, air and moisture, chloromethyl pivalate (0.27 ml, 1.8 mmol) was added to a solution of imine oxazoline **3a** (330 mg, 1.3 mmol) and silver triflate (395 mg, 1.5 mmol) in methylene chloride (10 ml) and the reaction vessel was sealed. After stirring with exclusion of light at 40°C for 16 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, and the filter residue was washed with methylene chloride (10 ml) and the filtrate concentrated. Purification of the residue by double column chromatography (2 × 10 cm, CH_2Cl_2 to 15:1 CH_2Cl_2/MeOH) gave the imidazolium triflate **4a** (432 mg, 80%).

$[a]^{20}_D$ = +19.5 (c 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 1.4 Hz, 1H, NCHN), 7.02 (s, 1H, CH_{ar}), 7.00 (s, 1H, CH_{ar}), 6.29 (d, *J* = 1.4 Hz, NCHC), 5.42-5.39 (m, 1H, C*H*CH_2), 5.29 (t, *J* = 8.7 Hz, 1H, CH_2), 4.99 (dd, *J* = 3.7, 9.2 Hz, 1H, CH_2), 2.54-2.47 (m, 1H, C*H*CH_3), 2.35 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 1.04 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$), 0.98 (d, J = 6.9 Hz, 3H, CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3 (C), 141.4 (C), 135.0 (C), 133.8 (C), 131.5 (C), 130.0 (CH_{ar}), 129.5 (CH_{ar}), 127.8 (NCHN), 120.6 (q, *J* = 320 Hz, CF_3), 95.4 (NCHC), 79.6 (CH_2), 63.1 (*C*HCH_2), 31.1 (*C*HCH_3), 21.1 (CH_3), 17.4 (CH_3), 17.2 (CH_3), 17.0 (CH_3), 16.2 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.7 (CF_3).

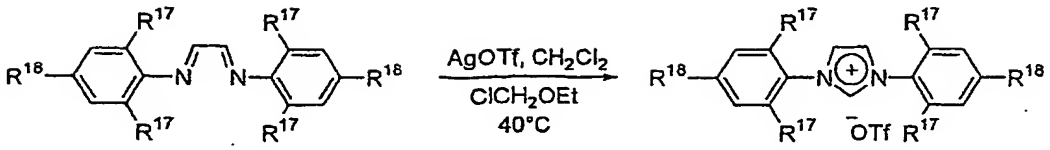
Example 5

Preparation of imidazolium triflate **4b**

In a flame dried and argonized Schlenk vessel, with exclusion of light, air and moisture, chloromethyl pivalate (0.42 ml, 2.8 mmol) was added to a solution of imine oxazoline **3b** (600 mg, 2.0 mmol) and silver triflate (617 mg, 2.4 mmol) in methylene chloride (17 ml) and the reaction vessel was sealed. After stirring with exclusion of light at 40°C for 16 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, and the filter residue was washed with methylene chloride (10 ml) and the filtrate concentrated. Purification of the residue by double column chromatography (2.5 × 10 cm, CH_2Cl_2 to 15:1 CH_2Cl_2/MeOH) gave the imidazolium triflate **4b** (771 mg, 83%).

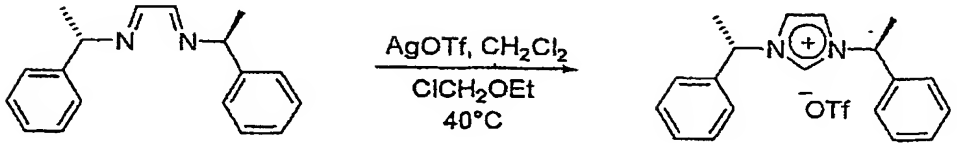
$[a]^{20}_D$ = +23.8 (c 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 1.5 Hz, 1H, NCHN), 7.55-7.51 (m, 1H, CH_{ar}), 7.33-7.27 (m, 2H, CH_{ar}), 6.33 (d, *J* = 1.5 Hz, NCHC), 5.47-5.43 (m, 1H, C*H*CH_2), 5.33 (t, *J* = 8.7 Hz, 1H, CH_2), 5.02 (dd, *J* = 3.6, 9.2 Hz, 1H, CH_2), 2.58-2.51 (m, 2H, C*H*CH_3), 2.32 (sept, *J* = 6.9 Hz, 1H, C*H*CH_3), 1.26 (d, *J* = 6.8 Hz, 3H, CH_3), 1.21 (d, *J* = 7.0 Hz, 3H, CH_3), 1.19 (d, *J* = 7.0 Hz, 3H, CH_3), 1.17 (d, *J* = 6.8 Hz, 3H, CH_3), 1.04 (d, *J* = 6.9 Hz, 3H, CH_3), 0.98 (d, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2 (C), 146.1 (C), 145.0 (C), 132.0 (CH_{ar}), 130.9 (C), 128.4 (NCHN), 125.0 (CH_{ar}), 124.3 (CH_{ar}), 120.6 (q, *J* = 320 Hz, CF_3), 96.7 (NCHC), 79.7 (CH_2), 63.2 (*C*HCH_2), 31.2 (CH), 28.8 (CH), 28.5 (CH), 24.5 (CH_3), 24.5 (CH_3), 23.9 (CH_3), 23.8 (CH_3), 17.3 (CH_3), 16.1 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.7 (CF_3).

Conversion of bisimines **5** to the corresponding imidazolium triflates **6** according to the following equations



5a: R^{17} = Me, R^{18} = Me
5b: R^{17} = iPr, R^{18} = H

6a: R^{17} = Me, R^{18} = Me
6b: R^{17} = iPr, R^{18} = H



5c

6c

Example 6

Preparation of 1,3-bis(2,4,6-trimethylphenyl)imidazolium triflate (**6a**)

In a flame dried and argonized Schlenk vessel, with the exclusion of light, air and moisture, chloromethyl ethyl ether (0.047 ml, 0.48 mmol) was added to a solution of bisimine **5a** (100 mg, 0.34 mmol) and silver triflate (105 mg, 0.41 mmol) in methylene chloride (2 ml), and the reaction vessel was sealed. After stirring with the exclusion of light at 40°C for 16 hours, the reaction mixture cooled to room temperature was filtered through a glass frit, the filter residue was washed with methylene chloride (2 ml) and the filtrate was concentrated. Purification of the residue by recrystallization from toluene gave the imidazolium triflate **6a** (129 mg, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (t, J = 1.4 Hz, 1H, NCHN), 7.56 (d, J = 1.4 Hz, 2H, NCHCHN), 7.03 (s, 4H, CH_{ar}), 2.35 (s, 6H, p-CH_3), 2.11 (s, 12H, o-CH_3; ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5 (C), 137.9 (NCHN), 134.0 (C), 130.4 (C), 129.9 (CH_{ar}), 124.9 (NCHCHN), 120.4 (q, J = 321 Hz, CF_3), 21.1 (p-CH_3), 17.2 (o-CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.9 (CF_3).

Example 7

Preparation of 1,3-bis(2,6-diisopropylphenyl)imidazolium triflate (**6b**)

In a flame dried and argonized Schlenk vessel, with the exclusion of light, air and moisture, chloromethyl ethyl ether (0.036 ml, 0.37 mmol) was added to a solution of bisimine **5b** (100 mg, 0.27 mmol) and silver triflate (82 mg, 0.32 mmol) in methylene chloride (1.5 ml), and the reaction vessel was sealed. After stirring with the exclusion of light at 40°C for 1 hour, the reaction mixture cooled to room temperature was filtered through a glass frit, the filter residue was washed with methylene chloride (2 ml) and the filtrate was concentrated. Purification of the residue by recrystallization from toluene gave the imidazolium triflate **6b** (116 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (t, J = 1.6 Hz, 1H, NCHN), 7.79 (d, J = 1.6 Hz, 2H, NCHCHN), 7.57 (t, J = 7.9 Hz, 2H, CH_{ar}), 7.34 (d, J = 7.9 Hz, 4H, CH_{ar}), 2.40 (sept, J = 6.8 Hz, 2H, CH), 1.26 (d, J = 6.8 Hz, 6H, CH_3), 1.20 (d, J = 6.8 Hz, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9 (C), 138.2 (NCHN), 132.1 (CH_{ar}), 129.7 (C), 126.3 (NCHCHN), 124.7 (CH_{ar}), 120.5 (q, J = 321 Hz, CF_3), 29.1 (CH), 24.2 (CH_3), 23.8 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.9 (CF_3).

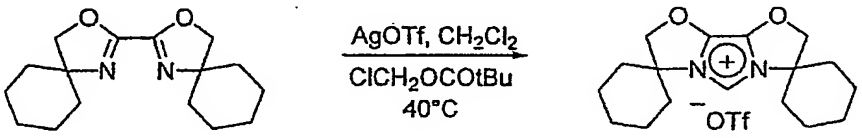
Example 8

Preparation of (S,S)-1,3-bis(1-phenylethyl)imidazolium triflate (**6c**)

In a flame dried and argonized Schlenk vessel, with the exclusion of light, air and moisture, chloromethyl ethyl ether (1.4 ml, 14.0 mmol) was added at 0°C to a solution of bisimine **5c** (2.6 g, 10.0 mmol) and silver triflate (3.1 g, 12.0 mmol) in methylene chloride (20 ml), and the reaction vessel was sealed. After stirring with the exclusion of light at 40°C for 1 hour, the reaction mixture cooled to room temperature was filtered through a glass frit, the filter residue was washed with

methylene chloride (20 ml) and the filtrate was concentrated. Purification of the residue by column chromatography (3.5 × 12 cm, CH_2Cl_2 to 15:1 CH_2Cl_2/MeOH) gave the imidazolium triflate **6c** (3.5 g, 81%).

$[a]^{20}_D$ = -21.5 (c 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.51 (t, *J* = 1.7 Hz, 1H, NCHN), 7.41-7.35 (m, 10H, CH_{ar}), 7.20 (d, *J* = 1.7 Hz, 2H, NCHCHN), 5.77 (q, *J* = 7.0 Hz, 2H, CH), 1.95 (d, *J* = 7.0 Hz, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6 (C), 134.6 (NCHN), 129.4 (CH_{ar},CH_{ar}), 126.9 (CH_{ar}), 120.8 (NCHCHN), 120.7 (q, *J* = 320 Hz, CF_3), 60.2 (CH), 20.8 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.5 (CF_3).



7 8

Example 9

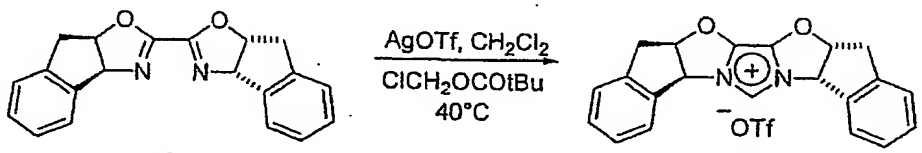
Preparation of imidazolium triflate **8**

In a Schlenk vessel, with the exclusion of light, air and moisture, chloromethyl pivalate (1.25 ml, 8.4 mmol) was added to a suspension of silver triflate (2.2 g, 8.4 mmol) in methylene chloride (30 ml) and the reaction solution was stirred for 45 minutes. After the solid formed had settled, the solution was introduced with a syringe into a second reaction vessel in which was disposed the bioxazoline **7** (1.6 g, 5.8 mmol). The solution was stirred at 40°C for 20 hours and the reaction mixture cooled to room temperature was subsequently concentrated under reduced pressure. Purification of the residue by column chromatography (2.5 × 10 cm, 20:1 to 10:1 CH_2Cl_2/MeOH) and subsequent recrystallization from a mixture of THF (10 ml), toluene (40 ml) and pentane (40 ml) gave the imidazolium triflate **8** (2.2 g, 85%) in the form of colorless crystals.

^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H, NCHN), 4.80 (s,

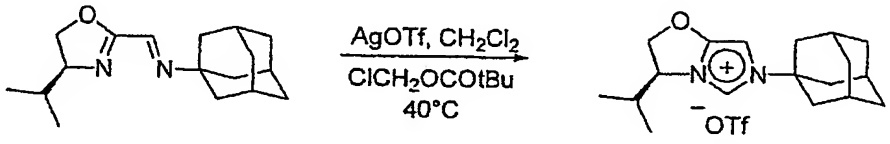
4H, OCH_2), 2.32 (td, J = 3.8, 12.5 Hz, 4H, CH_2), 2.10-1.98 (m, 8H, CH_2), 1.74-1.58 (m, 4H, CH_2), 1.46-1.37 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.6 (NCO), 120.8 (q, J = 319 Hz, CF_3), 113.9 (NCHN), 85.6 (OCH_2), 67.5 (CCH_2), 34.7 (CH_2), 23.5 (CH_2), 23.1 (CH_2); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.5 (CF_3).

The examples 10 to 13 were carried out in substantial analogy to the method specified for example 9:



9 10

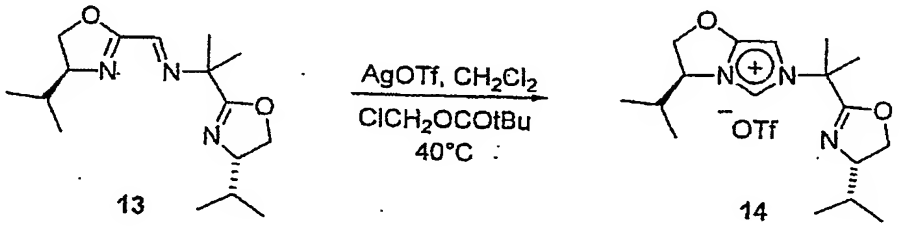
Example 10: Preparation of imidazolium triflate **10**.
3.4 g, 70%, colorless crystals; $[a]^{20}_D$ = +184.8 (c 0.9, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H, NCHN), 7.83 (d, J = 7.2 Hz, 2H, CH_{ar}), 7.40-7.28 (m, 6H, CH_{ar}), 6.32 (d, J = 6.4 Hz, 2H, CHN), 6.11-6.09 (m, 2H, CHO), 3.56-3.44 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6 (C), 134.8 (C), 130.8 (CH), 129.0 (CH), 126.1 (CH), 125.3 (CH), 124.9 (C), 120.7 (q, J = 320 Hz, CF_3), 114.4 (NCHN), 95.1 (OCH), 66.9 (NCHC), 38.3 (CH_2); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.6 (CF_3).



11 12

Example 11: Preparation of imidazolium triflate **12**.
1.2 g, 56%, white foam; $[a]^{20}_D$ = +25.9 (c 1.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 1.7 Hz, NCHN), 6.49 (d, J = 1.7 Hz, CH), 5.15-5.08 (m, 2H, CH & CH_2), 4.92-4.86 (m, 1H, CH_2), 2.47-2.38 (m, 1H, CH), 2.30 (s,

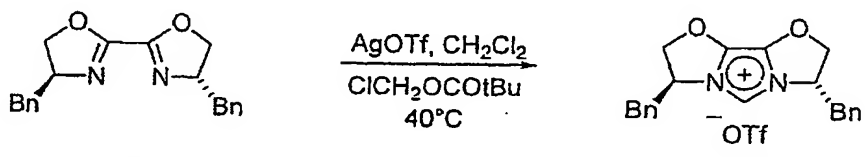
3H, CH), 2.13 (d, J = 2.9 Hz, 6H, CH_2), 1.78-1.76 (m, 6H, CH_2), 1.02 (d, J = 6.9 Hz, 3H, CH_3), 0.91 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1 (C), 124.5 (CH), 120.7 (q, J = 322 Hz, CF_3), 90.6 (CH), 79.2 (CH_2), 62.9 (CH), 61.3 (C), 42.6 (CH_2), 35.3 (CH_2), 30.9 (CH), 29.4 (CH), 17.8 (CH_3), 16.2 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.6 (CF_3).



13 14

Example 12: Preparation of imidazolium triflate **14**.

0.7 g, 56%, colorless oil; $[a]^{20}_D$ = -21.3 (c 1.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, J = 1.6 Hz, 1H, NCHN), 6.46 (d, J = 1.6 Hz, 1H, CH), 5.17-5.13 (m, 2H), 4.94-4.90 (m, 1H), 4.36 (dd, J = 8.6, 9.7 Hz, 1H), 4.06 (t, J = 8.2 Hz, 1H), 3.98-3.92 (m, 1H), 2.47-2.43 (m, 1H), 1.96 (s, 3H), 1.90 (s, 3H), 1.78-1.71 (m, 1H), 1.03 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4 (C), 150.8 (C), 126.4 (CH), 120.6 (q, J = 320 Hz, CF_3), 92.7 (CH), 79.3 (CH_2O), 72.2 (CHN), 71.8 (CH_2O), 63.0 (CHN), 61.5 (CMe_2), 32.4 (CH), 31.0 (CH), 26.0 (2 × CH_3), 18.5 (CH_3), 18.1 (CH_3), 17.6 (CH_3), 16.1 (CH_3); ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.6 (CF_3).



1d 2d

Example 13: Preparation of imidazolium triflate **2d**.

1.7 g, 36%, white foam; $[a]^{20}_D$ = +38.1 (c 1.4, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H, NCHN), 7.31-7.20 (m, 10H, CH_{ar}), 5.27-5.20 (m, 2H, CH), 5.00 (dd, *J* = 7.5, 9.1 Hz, 2H, CH_2), 4.75 (dd, *J* = 5.8, 9.0 Hz, 2H, CH_2), 3.40 (dd, *J* = 6.2, 13.9 Hz, 2H, CH_2Ph), 3.10 (dd, *J* = 8.1, 13.9 Hz, 2H, CH_2Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8 (C), 129.2 (CH), 129.2 (CH), 127.9 (CH_{ar}), 125.8 (C), 120.6 (q, *J* = 321 Hz, CF_3), 115.2 (NCHN), 81.0 (OCH_2), 59.7 (NCH), 38.5 (CH_2) δ^{19}F NMR (300 MHz, $CDCl_3$) δ -78.5 (CF_3).

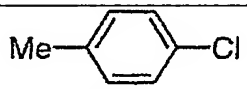
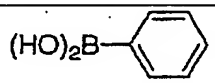
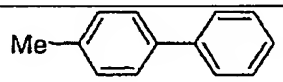
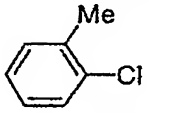
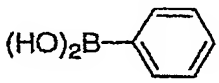
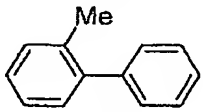
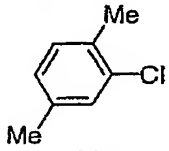
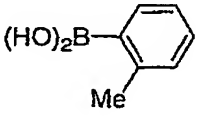
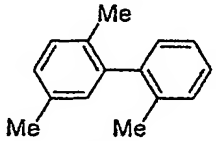
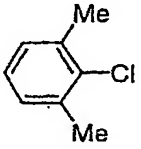
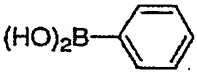
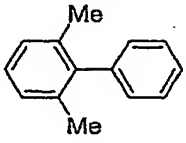
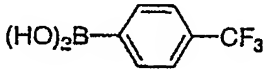
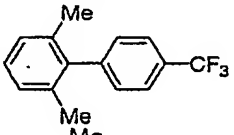
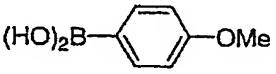
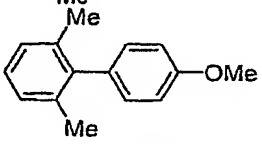
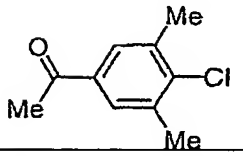
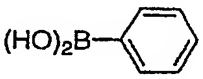
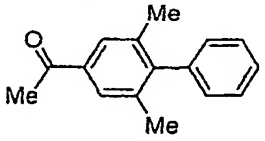
Working example for claim 22:

The Suzuki cross-coupling has become a standard synthetic method for biaryls in the academic and industrial sphere. (N. Miyaura, A. Suzuki, Chem. Rev. (1995) 95, 2457; S. Kotha, K. Lahiri, D. Kashinath, Tetrahedron (2002) 58, 9633.) While aryl iodides and bromides normally serve as substrates, the development of novel catalyst systems has recently also made it possible to efficiently couple the cheaper and more readily available aryl chlorides. (Review article: A.F. Littke, G.C. Fu, Angew. Chem. (2002) 114, 4350.) In spite of some effort, it has hitherto not been possible to couple aryl chlorides to biaryls having more than one ortho-substituent at room temperature. (Synthesis of sterically hindered biaryls by Suzuki cross-coupling at higher temperatures: J.P. Wolfe, R.A. Singer, B.H. Yang, S.L. Buchwald, J. Am. Chem. Soc. (1999) 121, 9550; A.F. Littke, C. Dai, G.C. Fu, J. Am. Chem. Soc. (2000) 122, 4020; J. Yin, M.P. Rainka, X.-X. Zhang, S.L. Buchwald, J. Am. Chem. Soc. (2002) 124, 1162.)

The use of a catalyst prepared from $Pd(OAc)_2$ and one equiv. of imidazolium salt **8** makes it possible to synthesize numerous biaryls from various aryl chlorides and arylboronic acids at room temperature. As shown in table 1, it is possible to couple unsubstituted, mono-ortho- and di-ortho-substituted aryl chlorides to a multitude of arylboronic acids in good to very good

yields, with turnover numbers of up to 1730 at room temperature. In addition, it is possible to couple the sterically hindered 2,6-dimethylbenzeneboronic acid with unsubstituted, ortho-substituted, electron-deficient and -rich aryl chlorides (table 2). These results constitute the first Suzuki cross-couplings of aryl chlorides and arylboronic acids for the preparation of di- and triortho-substituted biaryls at room temperature.

Table 1: Suzuki coupling of sterically hindered aryl chlorides.[a]

No.	Aryl chloride	Boronic acid	Product	Yield[b]
1				82%[c]
2				83%
3				94%
4				79%[c]
5	"			85%
6	"			87%
7				52%[d]
8				94%[e]

[a] Reaction conditions: 3 mol% of $Pd(OAc)_2$, **1** (prepared from 3.1 mol% of **2**, 6.25 mol% of KH, 0.67 mol% of KO*t*Bu in THF); 1.0 equiv. of aryl chloride (1 mmol), 1.1 equiv. of boronic acid, 2.0 equiv. of

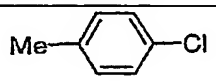
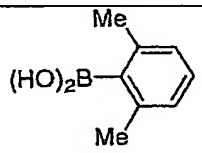
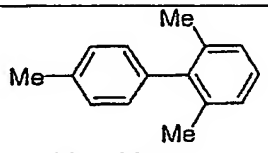
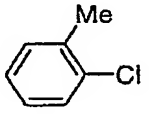
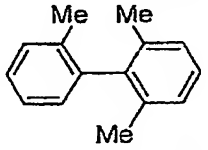
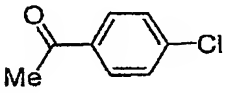
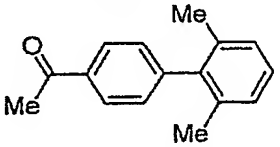
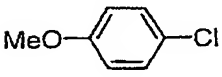
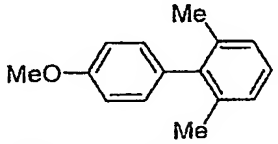
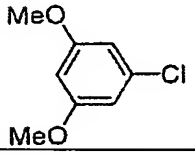
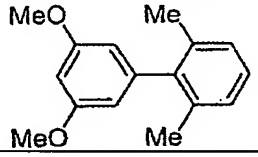
CsF, THF [0.3M], RT, 24 h. (Reaction times were not optimized).

[b] Isolated yield.

[c] <5% of product were obtained using **5** as a catalyst.

[d] 0.03 mol% of catalyst. [e] 0.03 mol% of catalyst, at 60°C.

Table 2: Suzuki coupling of sterically hindered boronic acids.[a]

No.	Aryl chloride	Boronic acid	Product	Yield[b]
1				70%
2		"		69%
3		"		95%
4		"		72%
5		"		76%

[a] Reaction conditions: 3 mol% of $Pd(OAc)_2$, **1** (prepared from 3.1 mol% of **2**, 6.25 mol% of KH, 0.67 mol% of KO*t*Bu in THF); 1.0 equiv. of aryl chloride (1 mmol), 1.1 equiv. of boronic acid, 2.0 equiv. of KO*t*Bu; THF/H_2O [10:1, 0.3 M], RT, 24 h (reaction times were not optimized).

[b] Isolated yield.

Comparative example 1

The synthesis of the chloride of an imidazolium salt **6a** was described in the literature with a yield of 40% after a reaction time of 5 days. (A.J. Arduengo, III, R. Krafczyk, R. Schmutzler, Tetrahedron (1999) 55, 14523.)

Comparative example 2

The synthesis of the chloride of an imidazolium salt **6b** was described in the literature with a yield of 47% after a reaction time of 16 hours. (A.J. Arduengo, III, R. Krafczyk, R. Schmutzler, Tetrahedron (1999) 55, 14523.)

Comparative example 3

The attempted synthesis of the chloride of an imidazolium salt **2a, 2b** and **2c** by the method described in the literature (A.J. Arduengo, III, R. Krafczyk, R. Schmutzler, Tetrahedron (1999) 55, 14523.) for bisimines gave a complex mixture of several products.